REMARKS

I. Status of the Claims

Claims 2, 20, 22, 56, 70, 71, 92, 101, 108, 110 and 118-120 have been amended. No claims have been canceled. Claims 2-15, 20-30, 53-56 and 70-120 currently pending.

Although the amendments to the claims that were entered to clarify the nature of the invention are addressed in respective sections below, Applicant points out that an additional amendment has been made to claim 101 to address an oversight on Applicant's part. In particular, the step of "providing nutrients to said host cells by perfusion or through a fed-batch process" has been added to claim 101. This language was discussed with the Examiner during the Examiner's interview in the context of other claims and was found to be acceptable in those contexts. Thus, this amendment should be acceptable in the context of claim 101 as well.

II. Examiner Interview

Applicant's undersigned representative met with the Examiner on July 27th, to discuss amendments and related issues that would place the case in condition for allowance. The present response reflects the claim amendments and related matters that were discussed at that time.

The Examiner additionally requested a copy of the priority provisional application 60/031,329, a copy of which is being provided to the Examiner by hand-delivery concurrently herewith.

III. **Rejection of Claims Under 35 USC 112, Second Paragraph**

The pending Action first rejected various claims which included the term "perfusion" as vague and indefinite based n comments made by Applicant's representative in the previous response which suggested that the term "perfusion" included fed-batch processes within its scope. Applicant apologizes for any confusion, and states on the record that the comments in this regard in the previous response were based upon a misinterpretation of the Examiner's comments in the previous Action. Applicant agrees that the term "perfusion" as normally used in the art and as used in the subject specification does not normally include "fed-batch" processes. The relevant claims have been amended to refer to "perfusion" and "fed-batch" in the alternative, which is believed to fully address the Examiner's concerns.

The Action next rejects various claims in their recitation of the phrase "essentially a single step," on the basis that the metes and bounds of "essentially" is not clear. In response, Applicant has amended the subject claims to remove the complained-of phrase "essentially," which amendment is submitted to fully address the Examiner's concerns.

Claims 56 and 71 have been amended to address the concerns relating to "said adaptation" and "less between."

Applicant submits that the foregoing amendments fully address the Examiner's various concerns under second paragraph of 35 USC 112.

IV. **Rejection of Claims Under 35 USC 112, First Paragraph**

The Action next rejects various of the claims under 35 USC 112, first paragraph, on the basis that the metes and bounds of the term "pharmaceutically acceptable" is not adequately described or enabled in the specification.

In response, Applicant notes that the specification fully and adequately describes the intended pharmaceutical compositi ns, and does indeed disclose a pharmaceutical composition, and methods of preparing such a pharmaceutical composition, that meets appropriate pharmaceutical criteria of purity and homogeneity (see, *e.g.*, pages 72-75, the examples pages 76-101, and in particular the tables at pages 87, 88, 93, 97 which evidence the high degree of purity obtainable using the processes of the present invention). Applicant submits that the Examiner's concerns are entirely misplaced and inappropriate, particularly in light of the fact that it is the purview of other branches of the government, most particularly the FDA, to consider issues of safety and pharmaceutical purity. Nevertheless, Applicants have broadened the claims to refer to simply "purified" compositions, a definition of which is contained in the specification at page 64, lines 7-15. This amendment should fully and adequately address the Examiner's concerns in this regard.

The Action next rejects various claims on the basis of language concerning "using a lysate technique other than freeze-thaw" for the purpose of preparing a lysate. In response, Applicant has amended the relevant claims to refer to specific lysing techniques. Support for these amendments can be found in original claims 16, 17, 59 and in the specification at pages 29-38.

V. Rejection of Claims 110-113, 115, and 116 Under 35 USC 102(b)

The Action next rejects claims 110-113, 115 and 116 as anticipated by Huyghe et al. on the basis that Huyghe et al. teaches that some degree of purification can be achieved using a single chromatography step.

In response, Applicant submits that Huyghe *et al.* clearly indicates that its teaching is directed to the use of two separate columns. For example, the Examiner's attention is directed to the PCT application corresponding to the Huyghe et al. reference, PCT application WO 96/27677 (reference B2) to Shabram et al.. At page 3, in the second sentence of the Summary section, the Shabram *et al.* PCT application makes it clear that two separate columns are contemplated as being required in order to prepare a purified viral vector for delivery of the therapeutic gene. It is submitted that such statements would lead one of skill in the art to conclude that at least two separate columns are required in order to obtain useful viral products.

Additionally, the subject claims have been amended to reflect a degree of recovery that is submitted to further distinguish Hyghe et al.. The claims now reflect a recovery of adenovirus following column chromatograph of 70% +/- 10% starting PFU. Support for this amendment can be found at page 12, line 5, Figure 23 and the paragraph bridging pages 99-100. This is a substantial improvement over Huyghe et al., who recover only 49% PFU after one column, and only 44% PFU following two columns (see table 2, page 1412).

In light of the foregoing, these claims should now be in condition for allowance.

VI. Rejection of Claims 101-104, 108, 110 and 115 Under 35 USC 102(e)

Lastly, the Action rejects claims 101-104, 108, 110 and 115 as anticipated by Munford under 35 USC 102(e).

In response, Applicant points out that the Munford patent teaches that adenovirus compositions are to be purified using cesium chloride gradients. However, Applicant's invention achieves appropriate purification of adenoviral compositions without the use of cesium chloride, relying instead upon, among other things, chromatographic techniques. One of the bases of

Applicant's invention is the purification of adenoviral compositions without the use of cesium chloride gradients. See, *e.g.*, specification at page 2, line 20, to page 3, line 11, and page 3, lines 28-29, and page 63, lines 11-15. Thus, the subject claims have been amended to exclude purification techniques that employ cesium chloride gradients for preparative purification. In light of these amendments, it is submitted that the subject claims are free of the cited art.

IV. Summary

In light of the foregoing amendments and remarks, applicant submits that all claims are in condition for allowance and solicit an early indication to this effect. Should Examiner Mosher have any questions regarding this response, she is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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